```
                5                  10                  15                  20
MetSerTyrAsnLeu LeuGlyPheLeuGln ArgSerSerAsnPhe GlnCysGlnLysLeu
               25                  30                  35                  40
LeuTrpGlnLeuAsn GlyArgLeuGluTyr CysLeuLysAspArg MetAsnPheAspIle
               45                  50                  55                  60
ProGluGluIleLys GlnLeuGlnGlnPhe GlnLysGluAspAla AlaLeuThrIleTyr
               65                  70                  75                  80
GluMetLeuGlnAsn IlePheAlaIlePhe ArgGlnAspSerSer SerThrGlyTrpAsn
               85                  90                  95                 100
GluThrIleValGlu AsnLeuLeuAlaAsn ValTyrHisGlnIle AsnHisLeuLysThr
              105                 110                 115                 120
ValLeuGluGluLys LeuGluLysGluAsp PheThrArgGlyLys LeuMetSerSerLeu
              125                 130                 135                 140
HisLeuLysArgTyr TyrGlyArgIleLeu HisTyrLeuLysAla LysGluTyrSerHis
              145                 150                 155                 160
CysAlaTrpThrIle ValArgValGluIle LeuAgAsnPheTyr PheIleAsnArgLeu
              165                 170                 175                 180
ThrGlyTyrLeuArg Asn---
```

FIG. 1

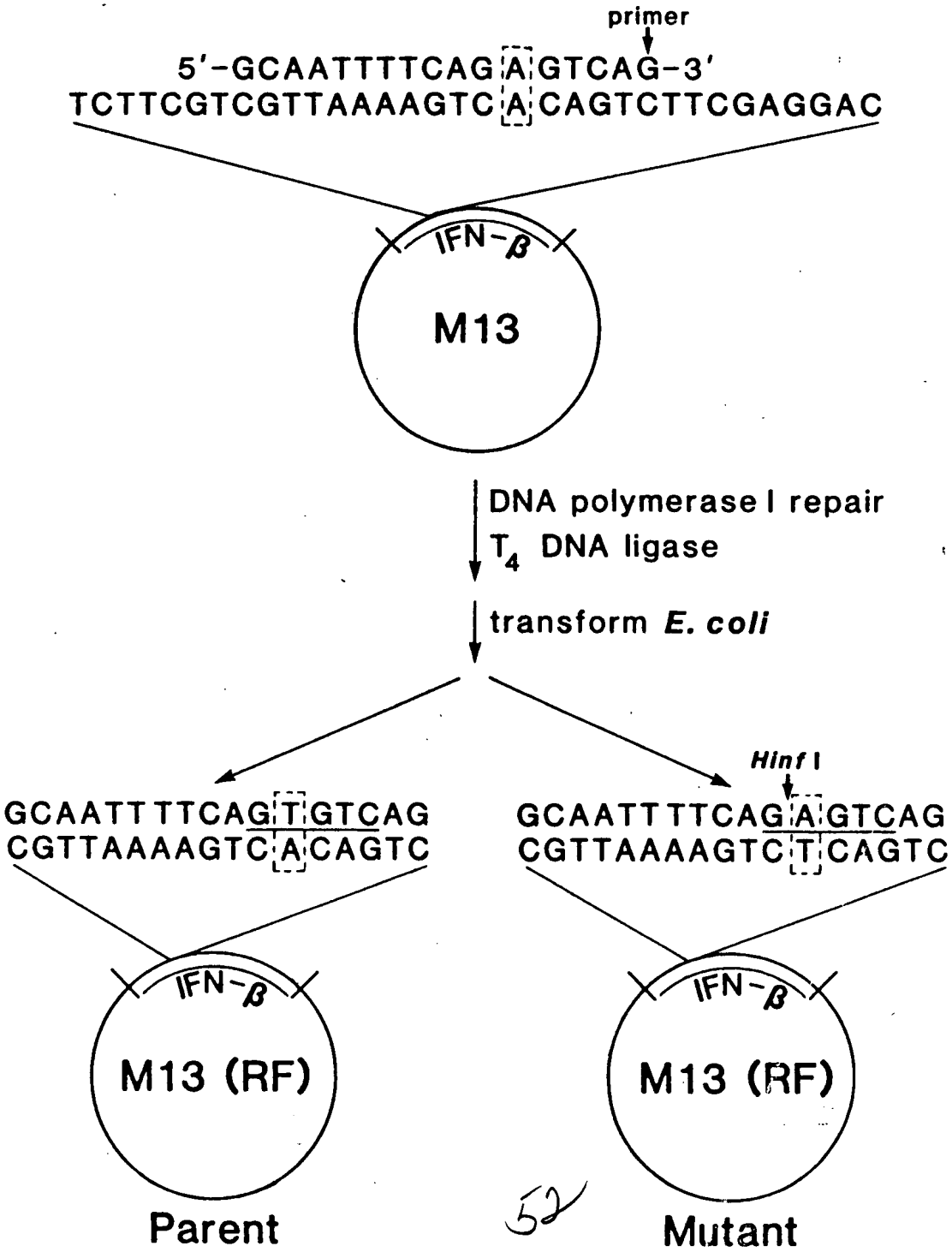

primer
5'-GCAATTTTCAGAGTCAG-3'
TCTTCGTCGTTAAAAGTCACAGTCTTCGAGGAC
IFN-β
M13
DNA polymerase I repair
T4 DNA ligase
transform E. coli
Hinf I
GCAATTTTCAGTGTCAG
CGTTAAAAGTCACAGTC
GCAATTTTCAGAGTCAG
CGTTAAAAGTCTCAGTC
IFN-β
M13 (RF)
IFN-β
M13 (RF)
Parent
Mutant

FIG. 2

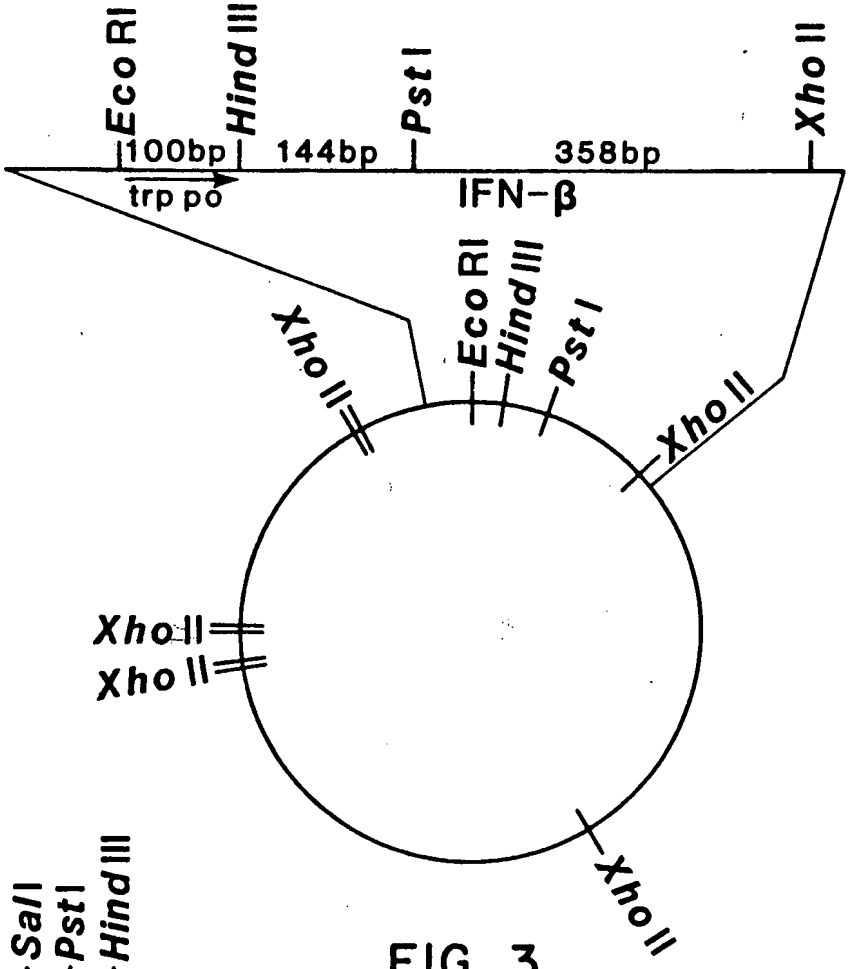

Eco RI
Hind III
Pst I
Xho II
100bp
144bp
358bp
trp po
IFN-β
Xho II
Eco RI
Hind III
Pst I
Xho II
Xho II
Xho II
Xho II

FIG. 3

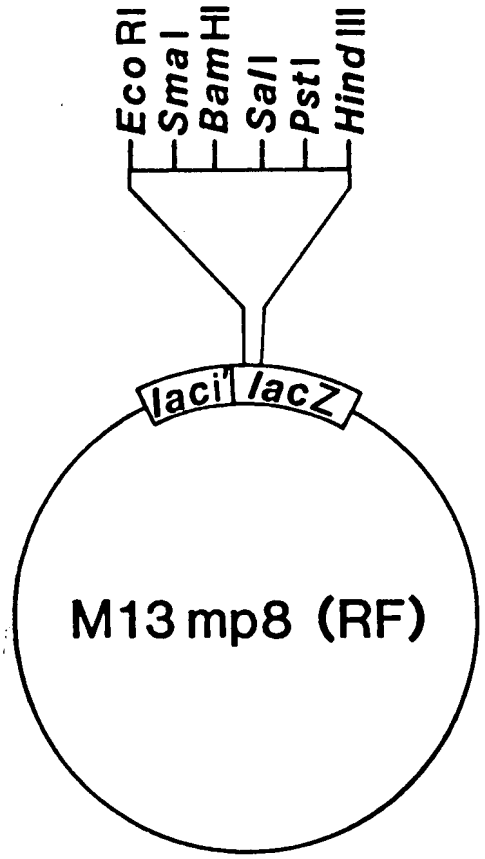

Eco RI
Sma I
Bam HI
Sal I
Pst I
Hind III
lacI
lacZ
M13 mp8 (RF)

FIG. 4

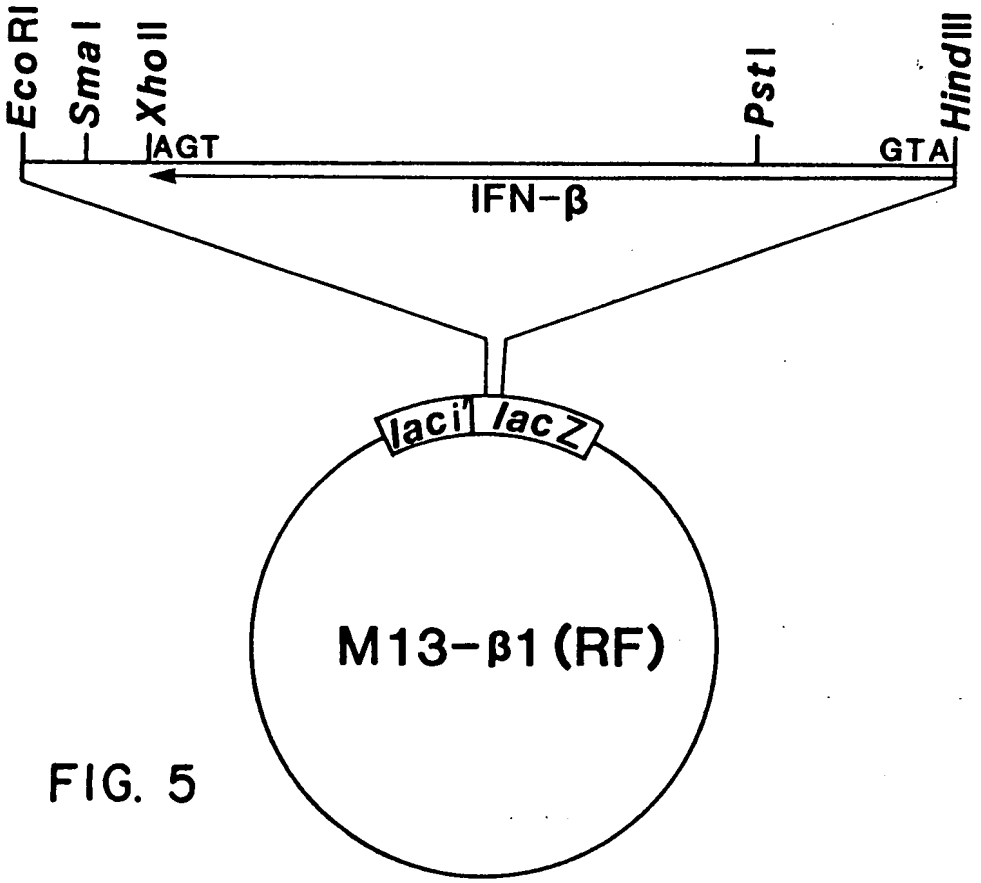

EcoRI
SmaI
XhoII
AGT
PstI
HindIII
GTA
IFN-β
lacI'
lacZ
M13-β1 (RF)

FIG. 5

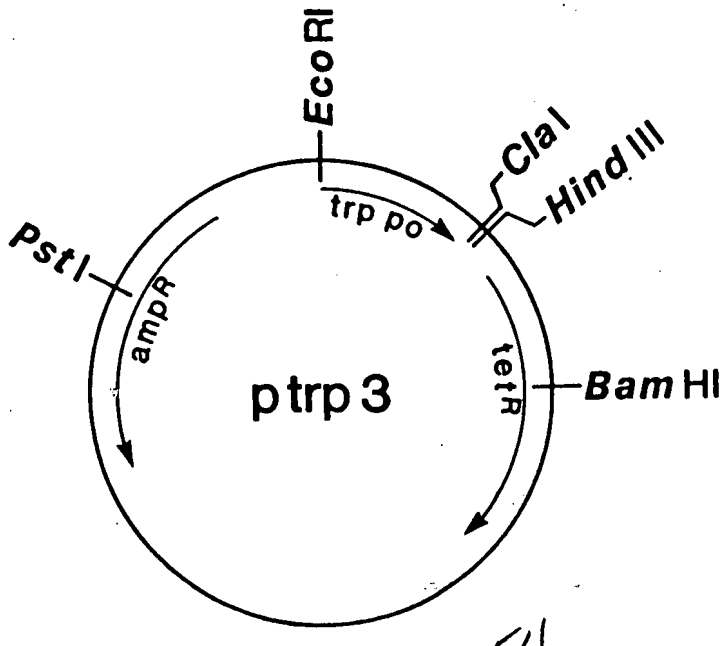
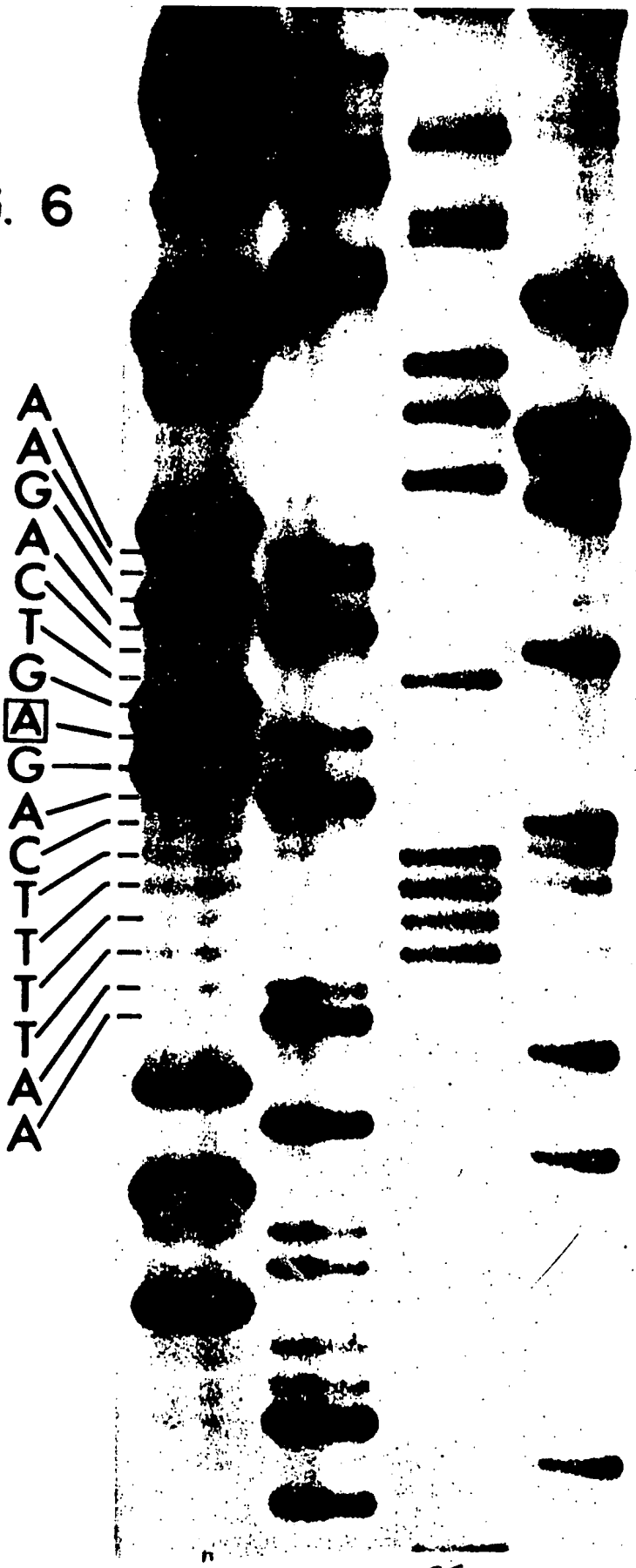

EcoRI
ClaI
HindIII
trp po
PstI
ampR
tetR
BamHI
ptrp3

FIG. 7

54

FIG. 6



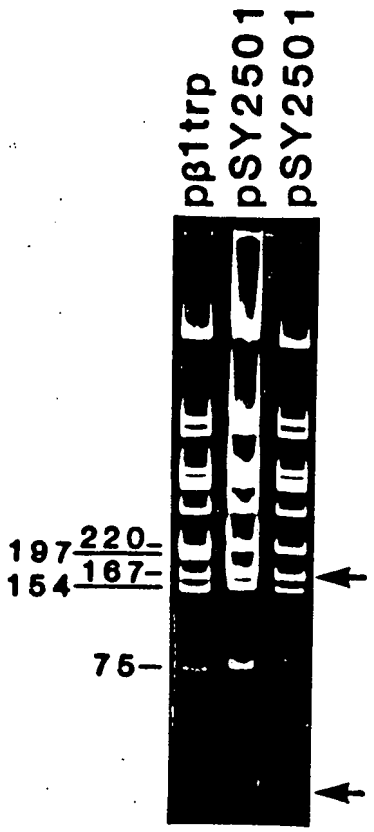

pβ1trp
pSY2501
pSY2501
197
220-
154
167-
75-

FIG. 8a

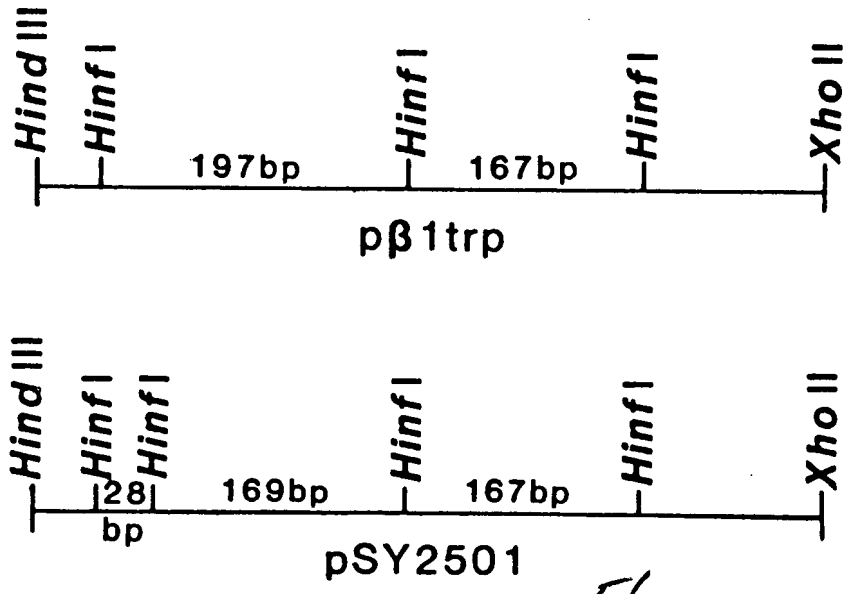

Hind III
Hinf I
197bp
Hinf I
167bp
Hinf I
Xho II
pβ1trp
Hind III
Hinf I
Hinf I
28
bp
169bp
Hinf I
167bp
Hinf I
Xho II
pSY2501

FIG. 8b

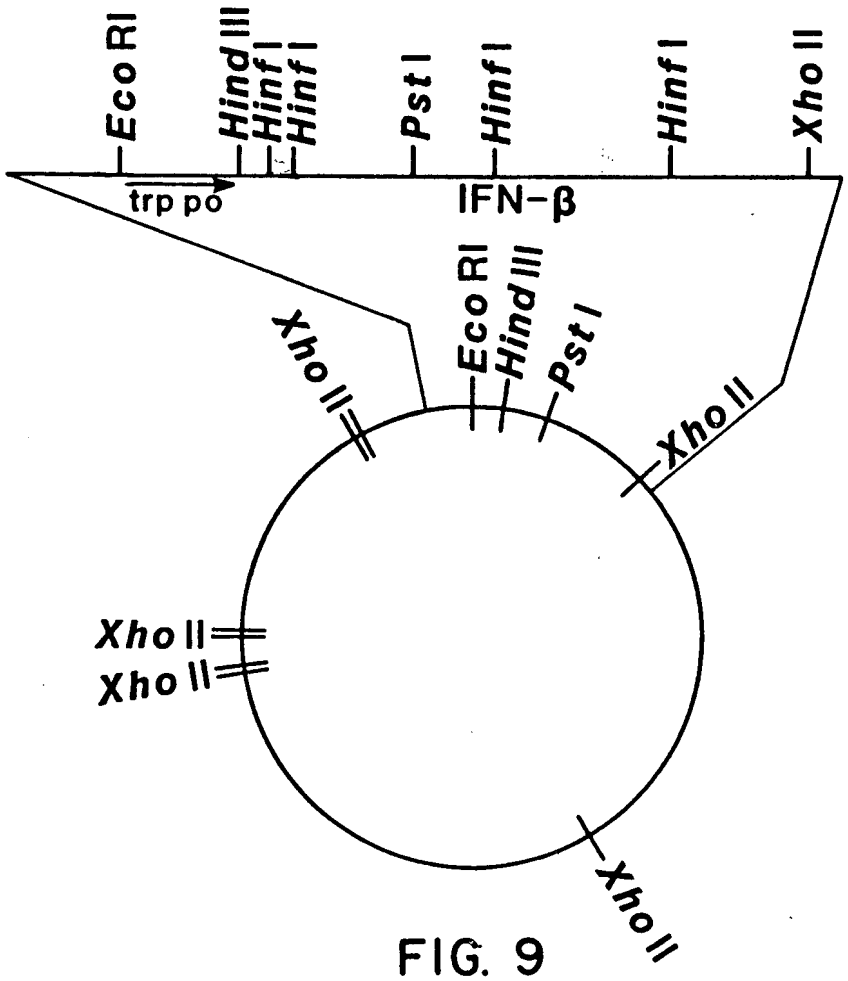

Eco RI
Hind III
Hinf I
Hinf I
Pst I
Hinf I
Hinf I
Xho II
trp po
IFN-β
Eco RI
Hind III
Pst I
Xho II
Xho II
Xho II
Xho II
Xho II

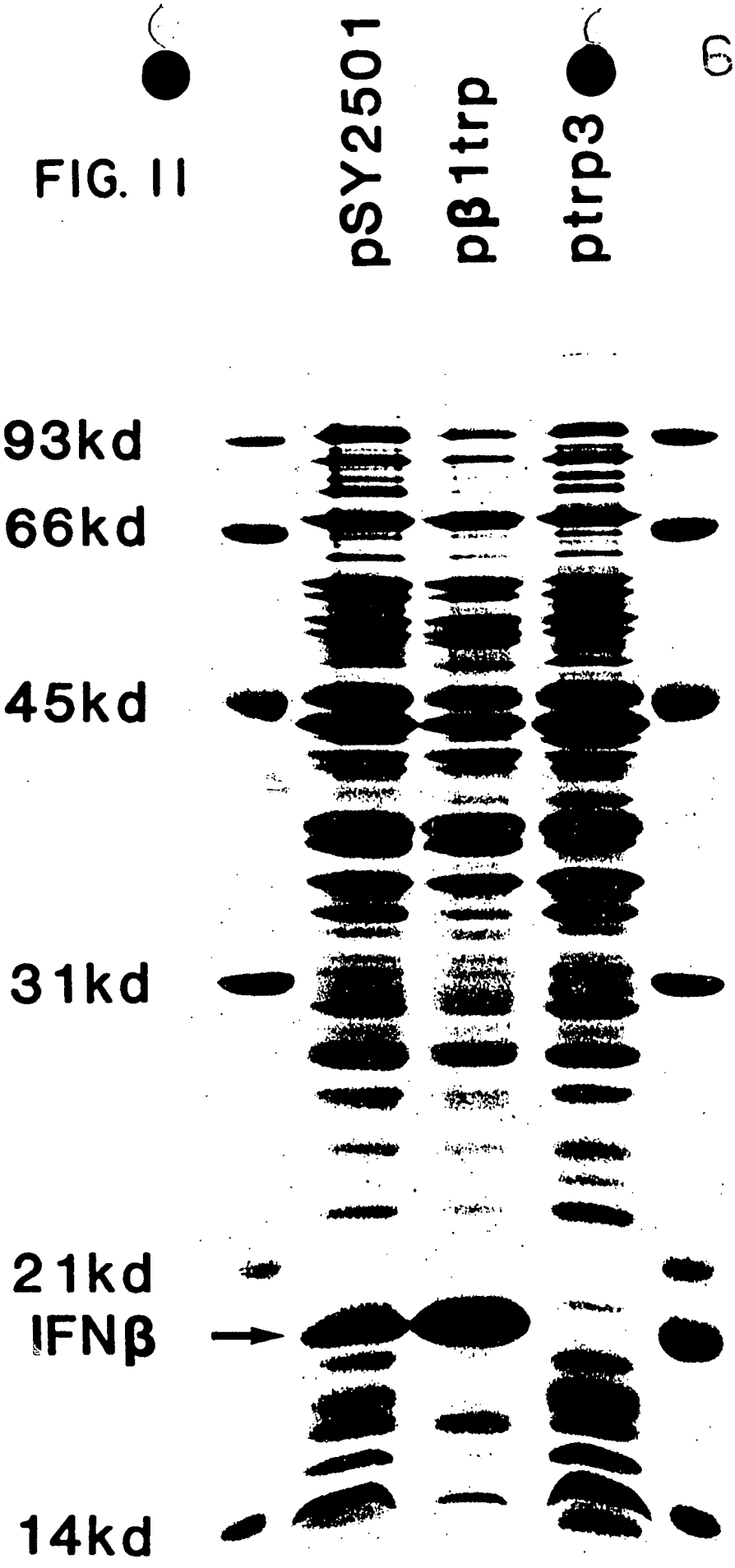
FIG. 9

IFN-B CYS TO SER CHANGE AT AMINO ACID 17

```
1                                                                   17
ATG AGC TAC AAC TTG CTT GGA TTC CTA CAA AGA AGC AGC AAT TTT CAG AGT CAG AAG CTC
met ser tyr asn leu leu gly phe leu gln arg ser ser asn phe gln ser gln lys leu

61
CTG TGG CAA TTG AAT GGG AGG CTT GAA TAT TGC CTC AAG GAC AGG ATG AAC TTT GAC ATC
leu trp gln leu asn gly arg leu glu tyr cys leu lys asp arg met asn phe asp ile

121
CCT GAG GAG ATT AAG CAG CTG CAG CAG TTC CAG AAG GAG GAC GCC GCA TTG ACC ATC TAT
pro glu glu ile lys gln leu gln gln phe gln lys glu asp ala ala leu thr ile tyr

181
GAG ATG CTC CAG AAC ATC TTT GCT ATT TTC AGA CAA GAT TCA TCT AGC ACT GGC TGG AAT
glu met leu gln asn ile phe ala ile phe arg gln asp ser ser ser thr gly trp asn

241
GAG ACT ATT GTT GAG AAC CTC CTG GCT AAT GTC TAT CAT CAG ATA AAC CAT CTG AAG ACA
glu thr ile val glu asn leu leu ala asn val tyr his gln ile asn his leu lys thr

301
GTC CTG GAA GAA AAA CTG GAG AAA GAA GAT TTC ACC AGG GGA AAA CTC ATG AGC AGT CTG
val leu glu glu lys leu glu lys glu asp phe thr arg gly lys leu met ser ser leu

361
CAC CTG AAA AGA TAT TAT GGG AGG ATT CTG CAT TAC CTG AAG GCC AAG GAG TAC AGT CAC
his leu lys arg tyr tyr gly arg ile leu his tyr leu lys ala lys glu tyr ser his

421
TGT GCC TGG ACC ATA GTC AGA GTG GAA ATC CTA AGG AAC TTT TAC TTC ATT AAC AGA CTT
cys ala trp thr ile val arg val glu ile leu arg asn phe tyr phe ile asn arg leu

481
ACA GGT TAC CTC CGA AAC TGA AGA TC
thr gly tyr leu arg asn *** 
```

FIG. 10

FIG. 11



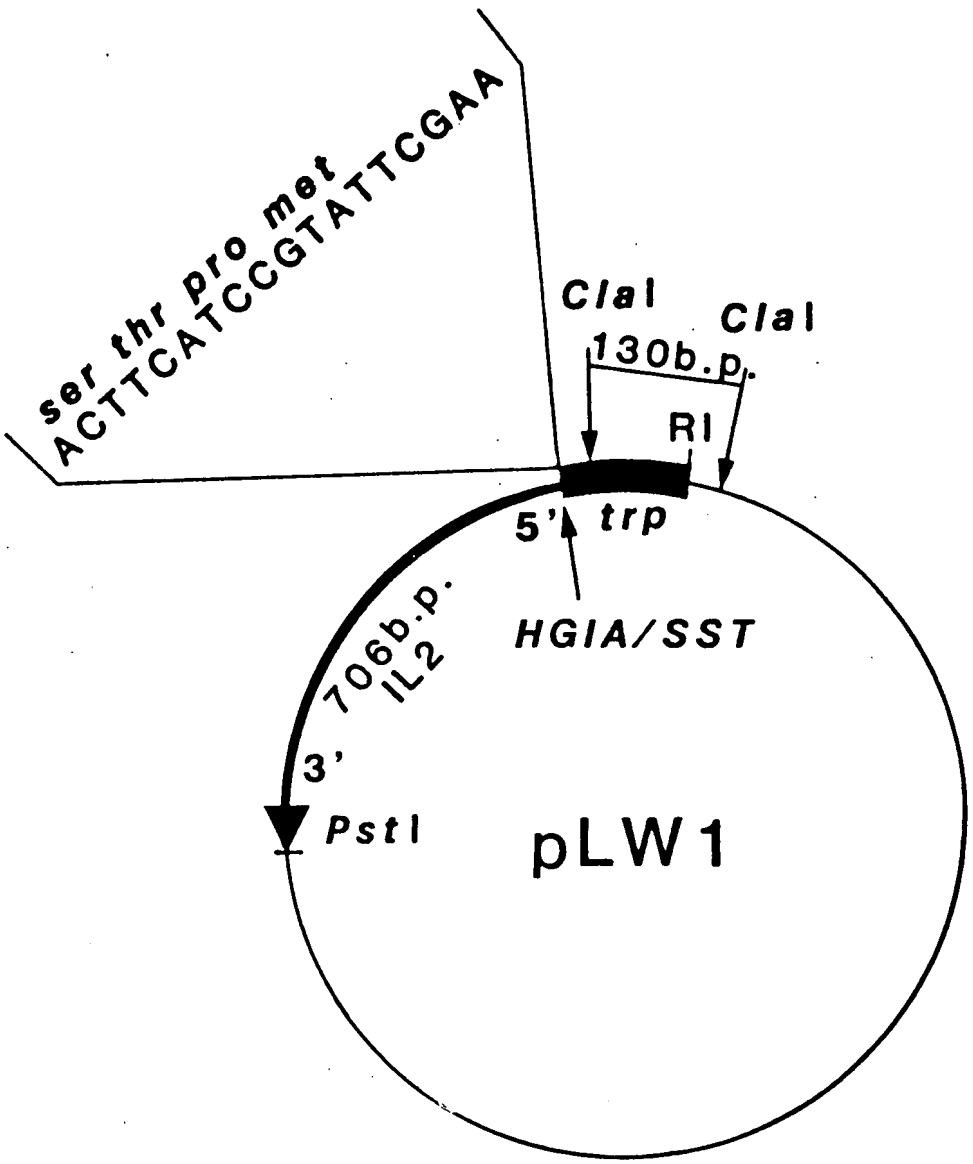

ser thr pro met
ACTTCATCCGTATTCGAA
ClaI
ClaI
130b.p.
RI
5'
trp
HGIA/SST
706b.p.
IL2
3'
PstI
pLW1

FIG. 12

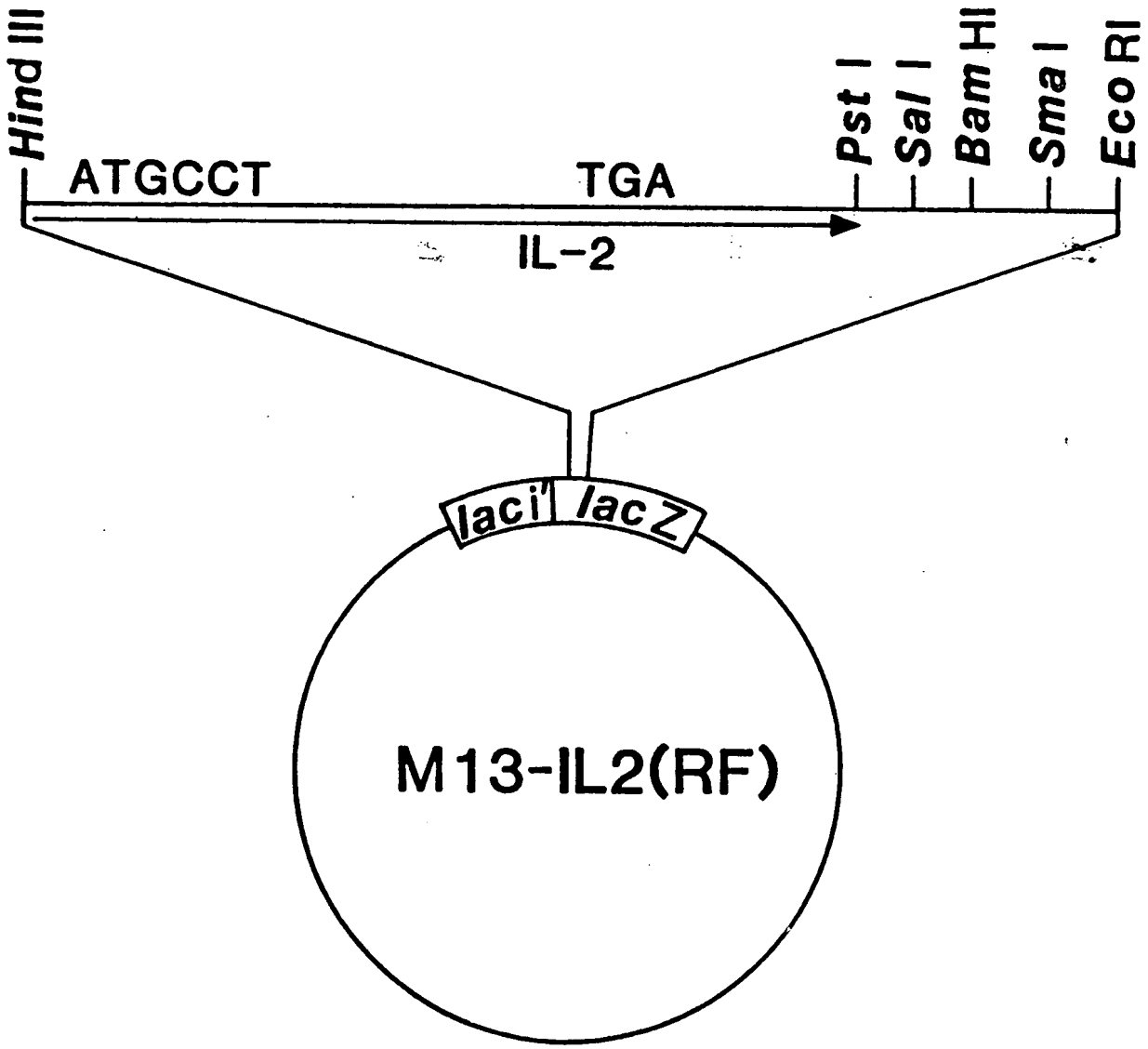

Hind III
ATGCCT
TGA
Pst I
Sal I
Bam HI
Sma I
Eco RI
IL-2
lacI'
lacZ
M13-IL2(RF)

FIG. 13

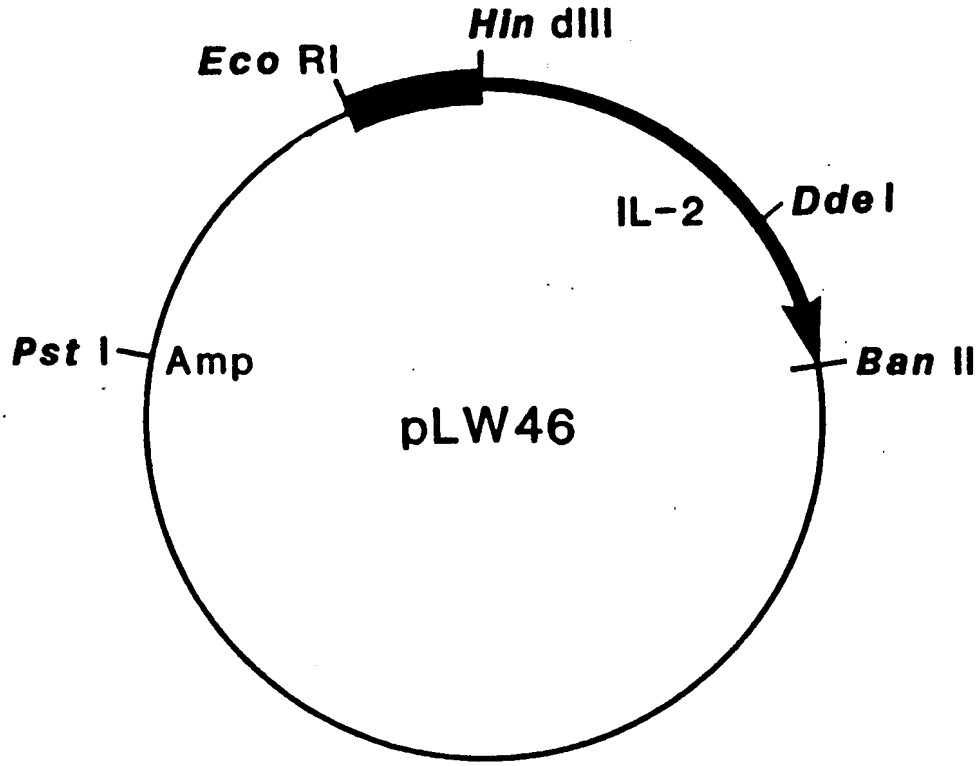


FIG. 14

```
        10          20          30          40          50          60
ATGCCTACTT CAAGTTCTAC AAAGAAAACA CAGCTACAAC TGGAGCATTT ACTGCTGGAT
        70          80          90         100         110         120
TTACAGATGA TTTTGAATGG AATTAATAAT TACAAGAATC CCAAACTCAC CAGGATGCTC
       130         140         150         160         170         180
ACATTTAAGT TTTACATGCC CAAGAAGGCC ACAGAACTGA AACATCTTCA GTGTCTAGAA
       190         200         210         220         230         240
GAAGAACTCA AACCTCTGGA GGAAGTGCTA AATTTAGCTC AAAGCAAAAA CTTTCACTTA
       250         260         270         280         290         300
AGACCCAGGG ACTTAATCAG CAATATCAAC GTAATAGTTC TGGAACTAAA GGGATCTGAA
       310         320         330         340         350         360
ACAACATTCA TGTGTGAATA TGCTGATGAG ACAGCAACCA TTGTAGAATT TCTGAACAGA
       370         380         390         400         410         420
TGGATTACCT TTTCTCAGAG CATCATCTCA ACACTGACTT GA
```

FIG. 15a

```
                5                  10                  15                  20
MetProThrSerSer SerThrLysLysThr GlnLeuGlnLeuGlu HisLeuLeuLeuAsp
               25                  30                  35                  40
LeuGlnMetIleLeu AsnGlyIleAsnAsn TyrLysAsnProLys LeuThrArgMetLeu
               45                  50                  55                  60
ThrPheLysPheTyr MetProLysLysAla ThrGluLeuLysHis LeuGlnCysLeuGlu
               65                  70                  75                  80
GluGluLeuLysPro LeuGluGluValLeu AsnLeuAlaGlnSer LysAsnPheHisLeu
               85                  90                  95                 100
ArgProArgAspLeu IleSerAsnIleAsn ValIleValLeuGlu LeuLysGlySerGlu
              105                 110                 115                 120
ThrThrPheMetCys GluTyrAlaAspGlu ThrAlaThrIleVal GluPheLeuAsnArg
              125                 130                 135                 140
TrpIleThrPheSer GlnSerIleIleSer ThrLeuThr---
```

FIG. 15b

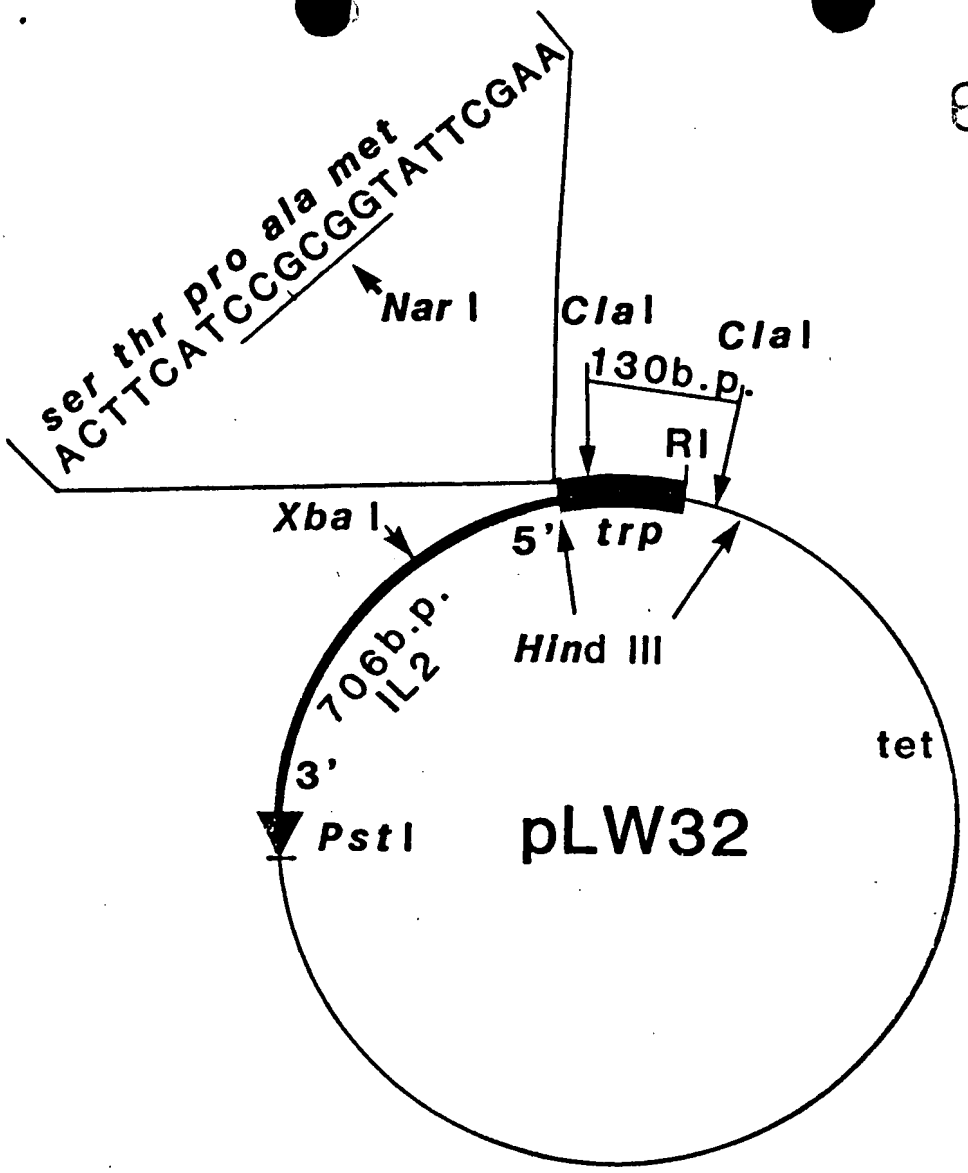


FIGURE 16

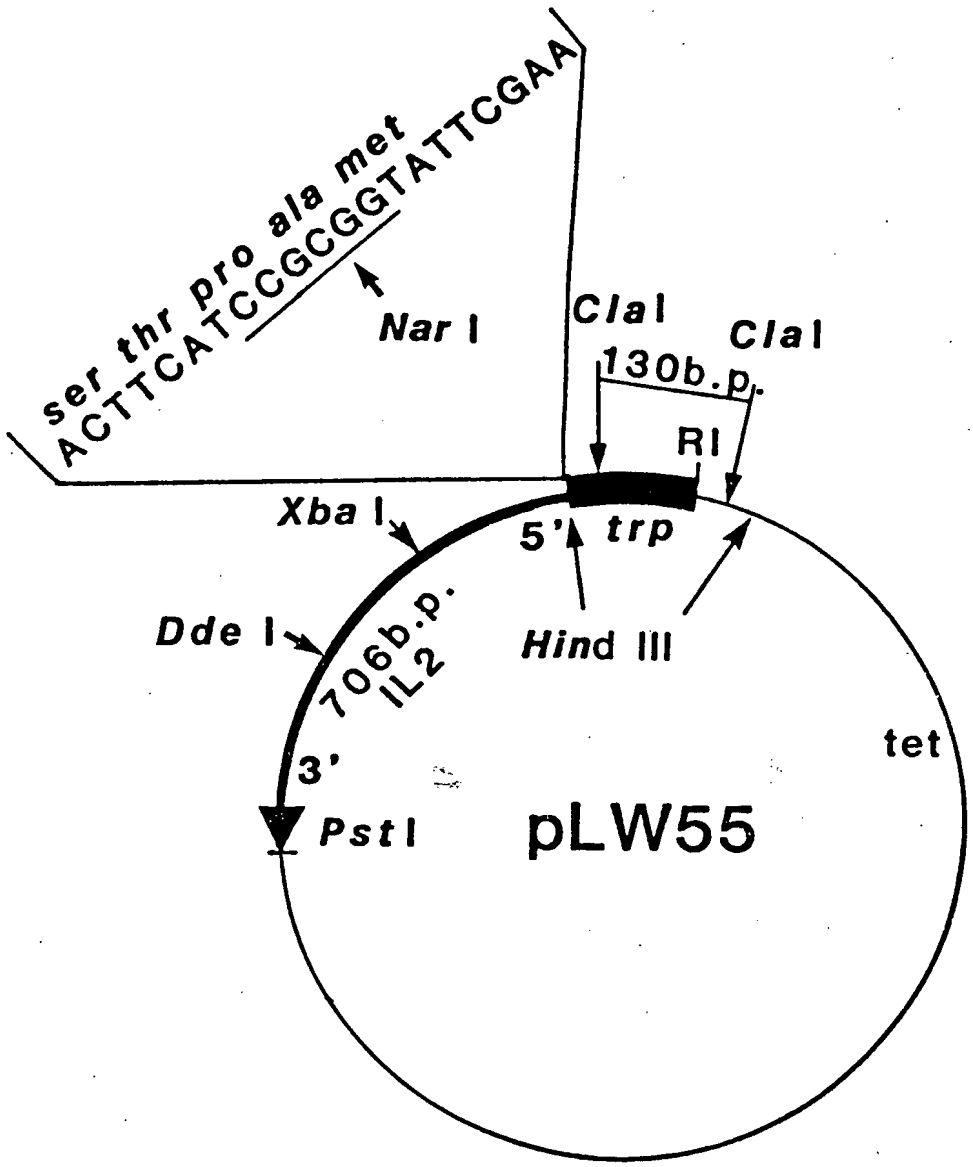


FIGURE 17